REMARKS

Applicant respectfully requests revival of this application and entry of this Amendment. The application presently stands abandoned for failing to respond to a PTO communication dated May 2, 2001. A petition to revive is submitted concurrently.

By way of background, the Applicant submitted a Response to Office Action on April 24, 2001. In a Notice of Non-Compliant Amendment dated May 2, 2001, Applicant was advised that the Response to Office Action did not comply with 37 C.F.R. § 1.121. Applicant thereafter submitted a Transmittal Letter to the Notice on May 9, 2001 that was deemed to be responsive to the Notice. But, it appears that the Transmittal Letter was either not received by the PTO or was deemed non-responsive, and a Notice of Abandonment issued on March 12, 2002. This Amendment substantially repeats the arguments and amendments originally presented in the paper dated April 24, 2001, and is formatted in compliance with 37 C.F.R. § 1.121.

Claims 1-74 are remaining in this application, with Claims 37-41, 73, and 74 withdrawn from consideration as directed to a non-elected invention. The specification and sequence listing are amended to correct a typographical error. Applicant respectfully requests reconsideration and review of the application as amended above.

The applicant contains a typographical error in that an extra "C" had been introduced into the NotI site of one set of anchor primers. The text, Figures 1, 2, and 8 and claims (e.g. claim 29) make it clear that the anchor primer contains a NotI site. One of ordinary skill would know that the sequence of the NotI site is a palindrome, i.e., G-C-G-G-C-C-G-C. The typographical error, G-C-G-G-C-**C**-C-G-C, would be recognized as an obvious error because it is not a palindrome, and not the NotI recognition site sequence. The typographical error is corrected in the amendments to the specification and sequence listing presented above. No new matter has been added to the application. See page 48 of the 1998/1999 New England Biolabs Catalog, attached hereto.

Claims 1, 8, 10-3 6 and 42-72 are rejected under 35 U.S.C. § 103(a) as

unpatentable over Erlander et al (WO 95/13369) in view of New England Biolabs catalog (page 11) (1993/1994 catalog). Applicant respectfully requests reconsideration and withdrawal of this rejection on the grounds that Erlander et al. alone or in combination with New England Biolabs catalog (page 11) (1993/1994 catalog) ("NEB"), neither teaches nor suggests the present claimed invention.

Claims 1-4, 8, 10-36 and 42-72 are rejected under 35 U.S.C. § 103(a) as unpatentable over Erlander et al (WO 95/13369) in view of New England Biolabs catalog (page 11) (1993/1994 catalog) and further in view of Kato et al. (EP 735 144 A1). As noted above, the combination of Erlander et al. and NEB does not teach or suggest the present invention. The addition of the Kato et al. reference does not cure this deficiency. Kato et al. teaches the ligation of biotinylated double stranded cDNA adapters to double stranded cDNA fragments produced by multiple digests with class IIS restriction enzymes. Applicants respectfully point out that the method of Erlander et al. lacks a step of ligation of double stranded cDNA adapters to double stranded cDNA fragments, and does not suggest the addition of such a step. Furthermore, the method of the present invention does not teach or claim the step of ligation of double stranded cDNA adapters to double stranded cDNA fragments. Thus, there would be no motivation for one of skill in the art to combine the teachings of the references to arrive at the present claimed invention.

Claims 1, 5-7, 8, 10-36 and 42-72 are rejected under 35 U.S.C. § 103(a) as unpatentable over Erlander et al (WO 95/13369) in view of New England Biolabs catalog (page 11) (I 993/1994 catalog) and further in view of Noronha et al (PCR Methods Appl (1992) 2:131-136). As noted above, the combination of Erlander et al. and NEB does not teach or suggest the present invention. The addition of the Noronha et al. reference does not cure this deficiency.

Claims 1, 8-36 and 42-72 are rejected under 35 U.S.C. § 103(a) as unpatentable over Erlander et al (WO 95/13369) in view of New England Biolabs catalog (page 11) (1993/1994 catalog) and further in view of Ju et al. (Anal. Biochem. (1995) 231:131-

140). As noted above, the combination of Erlander et al. and NEB does not teach or suggest the present invention. The addition of the Ju et al. reference does not cure this deficiency.

In view of the foregoing, the Applicant respectfully submits that all claims are in condition for allowance. Reconsideration and withdrawal of the rejections is respectfully requested, and a timely Notice of Allowability is solicited. To the extent it would be helpful to placing this application in condition for allowance, the Applicant encourages the Examiner to contact the undersigned counsel and conduct a telephonic interview.

Attached hereto is a marked-up version of the changes made to the specification and sequence listing by the current amendment. The attached pages are captioned **"Version with markings to show changes made."**

While Applicant believes that no additional fees are due in connection with the filing of this paper, the Commissioner is authorized to charge any shortage in the fees, including any extension of time fees, to Deposit Account No. 50-0639.

Respectfully submitted,

Date: April 19, 2002

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Registration No. 34,549

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Enclosure: 1998/1999 New England Biolabs Catalog (page 48)

Not I

RR NEB3 BSA 37° Yes!

NEBuffer	1	2	3	4
% Activity	0	75	100	50

#189S 500 units **$55**
#189L 2,500 units **$220**
order #189CL for high (5X) concentration

5′... GC▼GGCCGC...3′
3′... CGCCGG▲CG...5′

Source: An *E. coli* strain that carries the cloned *Not* I gene from *Nocardia otitidis-caviarum*

Reaction Buffer: NEBuffer 3 + BSA
100 mM NaCl, 50 mM Tris-HCl, 10 mM $MgCl_2$, 1 mM dithiothreitol (pH 7.9 @ 25°C). Supplement with 100 µg/ml BSA. Incubate at 37°C.

Ligation and Recutting: After 25-fold overdigestion with *Not* I, > 95% of the DNA fragments can be ligated and recut.

Concentration: 10,000 and 50,000 units/ml.
Assayed on Adenovirus-2 DNA.

Storage Conditions: 200 mM NaCl, 20 mM Tris-HCl (pH 7.4), 0.1 mM EDTA, 1 mM dithiothreitol, 0.15% Triton X-100, 200 µg/ml BSA, and 50% glycerol. Store at –20°C.

Diluent Compatibility: Diluent C, see page 66.

Heat Inactivation: 65°C for 20 minutes.

Note: Supercoiled plasmids may require up to 5-fold more *Not* I for complete digestion than linear DNAs.

Nru I

NEB4 37° dam Yes!

NEBuffer	1	2	3	4
% Activity	0	10	75	10

#192S 1,000 units **$44**
#192L 5,000 units **$176**
order #192CS or CL for high (5X) concentration

5′... TCG▼CGA...3′
3′... AGC▲GCT...5′

Source: *Nocardia rubra* (ATCC 15906)

Reaction Buffer: NEBuffer *Nru* I
100 mM KCl, 50 mM Tris-HCl, 10 mM $MgCl_2$, (pH 7.7 @ 25°C). Incubate at 37°C.

Ligation and Recutting: After 20-fold overdigestion with *Nru* I, less than 20% of the DNA fragments can be ligated.

Concentration: 10,000 and 50,000 units/ml.
Assayed on λ DNA.

Storage Conditions: 50 mM KCl, 10 mM Tris-HCl (pH 7.4), 0.1 mM EDTA, 1 mM dithiothreitol, 200 µg/ml BSA, and 50% glycerol. Store at –20°C.

Diluent Compatibility: Diluent A, see page 66.

Heat Inactivation: 65°C for 20 minutes.

Note: Blocked by overlapping *dam* methylation (see page 269).

Nsi I

RR NEB4 37° Yes!

NEBuffer	1	2	3	4
% Activity	25	25	50	10

#127S 1,000 units **$50**
#127L 5,000 units **$200**

5′... ATGCA▼T...3′
3′... T▲ACGTA...5′

Source: An *E. coli* strain that carries the cloned *Nsi* I gene from *Neisseria sicca* (NEB 913)

Reaction Buffer: NEBuffer *Nsi* I
100 mM NaCl, 10 mM Tris-HCl, 10 mM $MgCl_2$, 1 mM dithiothreitol (pH 8.4 @ 25°C). Incubate at 37°C.

Ligation and Recutting: After 50-fold overdigestion with *Nsi* I, > 95% of the DNA fragments can be ligated and recut.

Concentration: 10,000 units/ml.
Assayed on λ DNA.

Storage Conditions: 50 mM KCl, 10 mM Tris-HCl (pH 7.4), 0.1 mM EDTA, 1 mM dithiothreitol, 200 µg/ml BSA, and 50% glycerol. Store at –20°C.

Diluent Compatibility: Diluent A, see page 66.

Heat Inactivation: 65°C for 20 minutes.

Note: *Nsi* I is an isoschizomer of *Ava* III.

Nsp I

RR NEB2 BSA 37° Yes!

NEBuffer	1	2	3	4
% Activity	100	100	0	100

#602S 250 units **$50**
#602L 1,250 units **$200**

5′... PuCATG▼Py...3′
3′... Py▲GTACPu...5′

Source: An *E. coli* strain that carries the cloned *Nsp* I gene from *Nostoc* species C

Reaction Buffer: NEBuffer 2 + BSA
50 mM NaCl, 10 mM Tris-HCl, 10 mM $MgCl_2$, 1 mM dithiothreitol (pH 7.9 @ 25°C). Supplement with 100 µg/ml BSA. Incubate at 37°C.

Ligation and Recutting: After 10-fold overdigestion with *Nsp* I, > 95% of the DNA fragments can be ligated and recut.

Concentration: 5,000 units/ml.
Assayed on λ DNA.

Storage Conditions: 50 mM KCl, 10 mM Tris-HCl (pH 7.4), 0.1 mM EDTA, 1 mM dithiothreitol, 0.15% Triton X-100, 200 µg/ml BSA, and 50% glycerol. Store at –20°C.

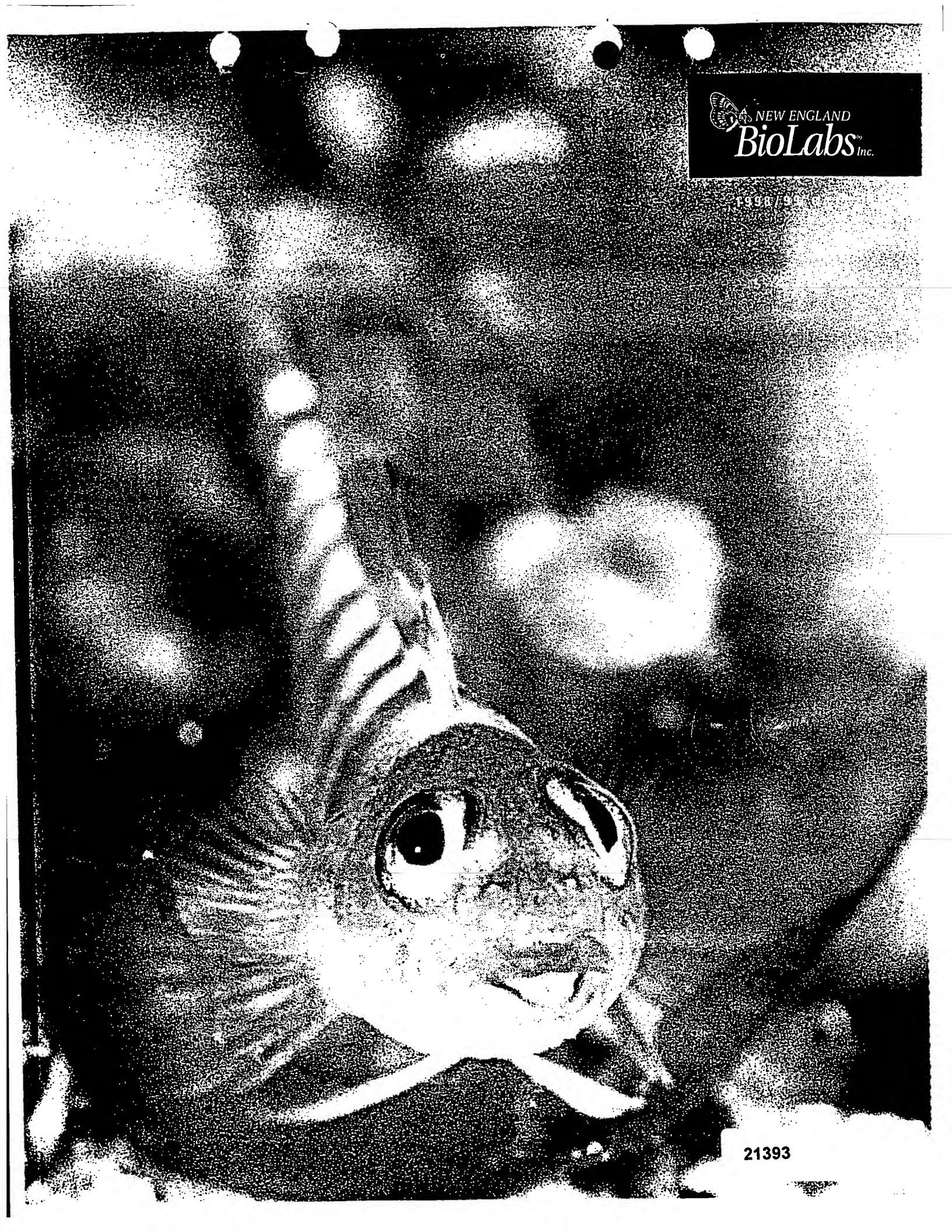
Diluent Compatibility: Diluent A, see page 66.

Note: *Nsp* I dilutions must be supplemented with 0.15% Triton X-100.

Heat Inactivation: 65°C for 20 minutes.

21392

Cloned at NEBiolabs RR Recombinant Enzyme NEB4 Optimum Buffer 37° Incubation Temperature


NEW ENGLAND
BioLabs Inc.
21393

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Paragraph beginning at line 27 of page 19 has been amended as follows:

Typically, the mixture of 48 anchor primers has the sequence A-A-C-T-G-G-A-A-G-A-A-T-T-C-G-C-G-G-C-C-G-C-A-G-G-A-A-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-V-N-N (SEQ ID NO: 5). In a preferred embodiment, the mixture of 48 anchor primers has the sequence G-A-A-T-T-C-A-A-C-T-G-G-A-A-G-C-G-G-C-C-[C-]G-C-A-G-G-A-A-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-V-N-N (SEQ ID N0: 8).

Paragraph beginning at line 3 of page 20 has been amended as follows:

Typically, the mixture of 12 anchor primers has the sequence A-A-C-T-G-G-A-A-G-A-A-T-T-C-G-C-G-G-C-C-G-C-A-G-G-A-A-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-V-N (SEQ ID NO: 4). In a preferred embodiment, the mixture of 12 anchor primers has the sequence G-A-A-T-T-C-A-A-C-T-G-G-A-A-G-C-G-G-C-C-[C-]G-C-A-G-G-A-A-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-V-N (SEQ ID NO: 7).

Paragraph beginning at line 9 of page 20 has been amended as follows:

Typically, the mixture of 3 anchor primers has the sequence A-A-C-T-G-G-A-A-G-A-A-T-T-C-G-C-G-G-C-C-G-C-A-G-G-A-A-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-V (SEQ ID NO: 3). In a preferred embodiment, the mixture of 3 anchor primers has the sequence G-A-A-T-T-C-A-A-C-T-G-G-A-A-G-C-G-G-C-C-[C-]G-C-A-G-G-A-A-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-T-V (SEQ ID NO: 6).

IN THE SEQUENCE LISTING:

Paragraphs beginning at line 8 of page 69 have been amended as follows:

<210> 6

<211> [47] 46

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:synthetic primer

<400> 6

gaattcaact ggaagcggcc [cgcaggaatt ttttttttt tttttv] gcaggaattt ttttttttt ttttv

<210> 7

<211> [48] 47

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:synthetic primer

<400> 7

gaattcaact ggaagcggcc [cgcaggaatt ttttttttt tttttvn] gcaggaattt ttttttttt ttttvn

<210> 8

<211> [49] 48

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:synthetic primer

<400> 8

gaattcaact ggaagcggcc [cgcaggaatt ttttttttt ttttttvnn] gcaggaattt ttttttttt tttttvnn